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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/600,272	06/20/2003	Robert G. Komeluk	07891/003006	3330

21559 7590 11/26/2004

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EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 11/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/600,272	KOMELUK ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *20 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed on 09/20/04 has been acknowledged.

Claims 1-21 are pending and are examined in this office action.

Applicants are required to follow Amendment Practice under revised 37 CFR §1.121. The fax phone numbers for the organization where this application or proceeding is assigned is ***703-872-9306****.*

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The references cited herein are of record in a prior Office action.

Double Patenting

Claims 1-21 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,656,704, for the same reasons of record as set forth in the office action mailed on 06/17/04.

The applicant argues that the applicants will submit such a disclaimer once allowable subject matter has been identified.

Claim Rejections - 35 USC § 112

Claims 1-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the

invention for the same reasons of record as set forth in the office action mailed on 06/17/04.

The scope of claims 1-7 encompasses any and all variants (95% identity) of SEQ ID NO: 24, 35, 26, 27, 40 (255-322) and 42 (241-308), wherein the variants are capable of inhibiting apoptosis of a mammalian cell. The scope claims 8-14 encompasses polypeptides that consists of amino acid sequences selected from SEQ ID NO: 24, 35, 26, 27, 40 (255-322) and 42 (241-308), wherein the polypeptide is capable of inhibiting apoptosis of a mammalian cell. The scope of claims 15-21 encompasses a polypeptide that comprises the amino acid sequence selected from SEQ ID NO: 24, 35, 26, 27, 40 (255-322) and 42 (241-308), wherein the polypeptide inhibits apoptosis in a mammalian cell. At best the specification as filed discloses a polypeptide of SEQ ID NO: 10, 4, 6, 8, 40 and 42 that are capable of inhibiting apoptosis of a mammalian cell (spec pages 27-33). The specification discloses that amino acid sequences of SEQ ID NO: 24, 25, 26, 27, 40 (255-322) and 42 (241-308) represent BIR-3 domain found in SEQ ID NO: 10 (mXIAP), 4(XIAP), 6(HIAP1), 8(HIAP2), 40(mHIAP1) and 42(mHIAP2) respectively (spec. page 23, table-2). However, the specification as filed fails to disclose any polypeptide that consists of amino acid sequences of SEQ ID NO: 24, 35, 26, 27, 40 (255-322) and 42 (241-308) is capable of inhibiting apoptosis of a mammalian cell. Specifically the specification fails to disclose that BIR-3 domain alone or any variant thereof (SEQ ID NO: 24, 35, 26, 27, 40 (255-322) and 42 (241-308)) is capable of inhibiting apoptosis in any kind of mammalian cell. In addition besides the polypeptides of SEQ ID NO: 10 (mXIAP), 4(XIAP), 6(HIAP1), 8(HIAP2), 40(mHIAP1) and 42(mHIAP2), the instant specification fails to disclose any other polypeptide that comprises the BIR3 domain (as claimed) and is capable of inhibiting apoptosis of a mammalian cells.

Response to arguments

The applicant argues that claims 8-14 are directed to polypeptides consisting of one of six sequences, which encode BIR-3 from human or mouse XIAP, HIAP-I, or HIAP-2, wherein the polypeptide is capable of inhibiting apoptosis when expressed in a

mammalian cell. The applicants assert that claims 8-14 are enabled, as demonstrated by a careful examination of the Wands factors. The claims are narrowly drawn to six polypeptides, the specification teaches how to make the polypeptides and test them for apoptosis-inhibiting activity, and at least one of the six has been shown to have a caspase-inhibiting activity, which is generally believed to be the mechanism by which IAP polypeptides inhibit apoptosis.

However, this is found not persuasive, since the specification as filed fails to disclose that isolated amino acid sequences that encodes BIR-3 domain alone SEQ ID NO: 24, 35, 26, 27, 40 (255-322) and 42 (241-308) are capable of inhibiting apoptosis of mammalian cell when the BIR-3 polypeptides as claimed are expressed in the mammalian cell. At best pages 29-30 and fig-15A of instant application discloses comparison of cell survival following transfection of full-length and partial IAP gene constructs but fall short of establishing that isolated amino acid sequences that encodes BIR-3 domain alone (i.e. SEQ ID NO: 24, 35, 26, 27, 40 (255-322) and 42 (241-308)) are capable of inhibiting apoptosis of a mammalian cell. The earlier office action clearly provide the evidence that although all IAP family proteins require at least one BIR domain for their anti-apoptotic function, it should be emphasized that not all BIR-containing proteins are necessarily involved in apoptosis regulation as indicated by the failure of the Ac-IAP protein to suppress apoptosis despite harboring a BIR domain. For example BIR1 and BIR3 domains of XIAP apparently lack caspase-binding capability, despite their striking amino acid similarity to BIR2 (42% for BIR1; 32% for BIR3). Assuming these results cannot be ascribed to trivial explanations such as misfolding of protein fragments taken out of their normal context of the intact protein, these observations suggest that not all BIR domains are created equal. Thus, it is plausible that even BIR domains within the same protein may have distinct functions (see Deveraux et al Gene & Dev. 13(3): 239-252, 1999).

The applicant further argues that claims 15-21 differ from claims 8-14, in that the claimed polypeptides include a BIR-3 domain, rather than consisting of a B1R3 domain alone. The applicant argues that in view of Sun et al and Takahashi et al invention as claimed is not unpredictable since the cited references teaches that a fusion protein

containing BIR2 domain can maintain caspase-inhibiting activity. The applicant argues that it would not require an undue amount of experimentation to make and test polypeptides containing one of six domains. Regarding the scope of claims 1-7 (95% variation in BIR3 domain) the applicant argues that a considerable amount of testing is permissible if it is routine in the art.

However this is fount not persuasive. The scope invention as claimed encompasses any and all polypeptides (natural or non-natural isolated from any organism) that includes a BIR-3 domain, wherein the polypeptide is capable of inhibiting apoptosis of mammalian cell. At best Takahashi teaches a fusion protein containing BIR2 domain can maintain caspase-inhibiting activity but fails to disclose such finding in context with BIR-3 domain especially in the inhibition of apoptosis. Furthermore making and testing a point mutation is significantly different from the making and testing an amino acid sequences wherein 5% amino acids are added, deleted and/or substituted. The number of possible scenario increase geometrically with increase in percent non-identity. Such making and testing is nothing more than an invitation to further experimentation, since the specification can not be relied on to teach how to make the variants as claimed. Therefore considering the applicant's disclosure and the state of the art (see Deveraux et al Gene & Dev. 13(3): 239-252, 1999) one has to engage in extensive making and testing in order to obtain variants that meet the requirements for the claimed inhibition of apoptosis activity. The disclosure "shall inform how to use, not how to find out how to use for themselves." See In re Gardner 475 F.2d 1389, 177 USPQ 396 (CCPA 1973). At issue, under the enablement requirement of 35 U.S.C. 1 12, first paragraph is whether, given the Wands-factors, the experimentation was undue or unreasonable under the circumstances. "Experimentation must not require ingenuity beyond that to be expected of one of ordinary skill in the art." See Fields v. Conover, 443 F.2d 1386, 170 USPQ 276 (CCPA 1970). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed, since applicant has not presented enablement commensurate in scope with the claims.

Claims 1-7 and 15-21 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons of record as set forth in the office action mailed on 06/17/04.

The scope of claims 1-7 encompasses any and all variants (95% identity) of SEQ ID NO: 24, 25, 26, 27, 40 (255-322) and 42 (241-308), wherein the variants are capable of inhibiting apoptosis of a mammalian cell. The scope of claims 15-21 encompasses any natural or non-natural polypeptides that comprises the amino acid sequence selected from SEQ ID NO: 24, 25, 26, 27, 40 (255-322) and 42 (241-308), wherein the polypeptides are capable of inhibiting apoptosis in a mammalian cell. At best the specification as filed discloses polypeptides of SEQ ID NO: SEQ ID NO: 10, 4, 6, 8, 40 and 42 that are capable of inhibiting apoptosis of a mammalian cell. Besides the polypeptides of SEQ ID NO: 10 (mXIAP), 4(XIAP), 6(HIAP1), 8(HIAP2), 40(mHIAP1) and 42(mHIAP2), the instant specification fails to disclose any other polypeptide that comprises the BIR-3 domain (as claimed) is capable of inhibiting apoptosis of a mammalian cells. Similarly the specification fails to disclose any variant of SEQ ID NO: 24, 25, 26, 27, 40 (255-322) and 42 (241-308) that are capable of inhibiting apoptosis of a mammalian cell.

Response to arguments

The applicant argues that the specification does disclose BIR domain-containing fragments and not simply full-length polypeptides. The applicant argues that MPEP states that there MAY be situations where one species adequately support a genus. The applicant further argues that invention as claimed satisfies the written description requirements in view of Revised Interim Written Description Guidelines Training Material guidelines.

However, applicant's argument are found NOT persuasive. Applicant was referred to the guidelines for ***Written Description Requirement*** published January 5, 2001 in the Federal Register, Vol.66, No.4, pp.1099-1110 (see http://www.uspto.gov).

As stated earlier the disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal 113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In the instant case besides disclosing the polypeptides of SEQ ID NO: 10 (mXIAP), 4(XIAP), 6(HIAP1), 8(HIAP2), 40(mHIAP1) and 42(mHIAP2), the instant specification fails to disclose any other polypeptide that comprises the BIR-3 domain (as claimed) and are capable of inhibiting apoptosis of a mammalian cells explicitly or implicitly as putatively claimed herein by the applicant (spec page 20, page 23 table-2, pages 27-33).

The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991)* In the instant case the amino acid sequences consisting of variants of SEQ ID NO: 24, 25, 26, 27, 40 (255-322) and 42 (241-308) or polypeptide comprising BIR-3 domains (as claimed) has been defined only by a statement of function that broadly encompasses inhibition of apoptosis in a mammalian cell, which conveyed no distinguishing information about the identity of the claimed polypeptide sequences, such as its relevant structural or physical characteristics. Furthermore the state of the art at the time of filing teaches that although all IAP family proteins require at least one BIR domain for their anti-apoptotic function, it should be emphasized that not all BIR-containing proteins are necessarily involved in apoptosis regulation as indicated by the failure of the Ac-IAP protein to suppress apoptosis despite harboring a BIR domain. For example, BIR1 and BIR3 domains of XIAP apparently lack caspase-binding capability, despite their striking amino acid similarity to BIR2 (42% for BIR1; 32% for BIR3). Assuming these results cannot be ascribed to trivial explanations such as misfolding of protein fragments taken out of their normal context of the intact protein, these

observations suggest that not all BIR domains are created equal. Thus, it is plausible that even BIR domains within the same protein may have distinct functions see Deveraux et al (Gene & Dev. 13(3): 239-252, 1999). According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 571-272-0769. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 571-272-0781.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to ***(571) 272-0547.*** For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199. The fax phone number for the organization where this application or proceeding is assigned is **703-872-9306.**

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

Sumesh Kaushal
Examiner GAU 1636

JEFFREY FREDMAN
PRIMARY EXAMINER
11/27/07